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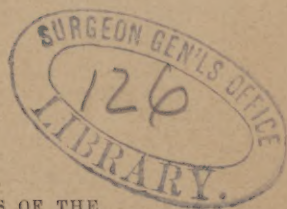
PRESENT CONDITION

OF THE

EVIDENCE CONCERNING DISEASE-GERMS.

BY

THOMAS E. SATTERTHWAITE, M.D.,  
OF NEW YORK.



EXTRACTED FROM THE TRANSACTIONS OF THE  
INTERNATIONAL MEDICAL CONGRESS,  
PHILADELPHIA, SEPTEMBER, 1876.

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THOMAS N. SATTLEWORTH, M.D.

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THE object of this paper is to give a sketch of the prominent theories now held as to the nature of disease-poisons. It seems hardly necessary for me to say that the short space of time at my disposal will prevent me from attempting to furnish either a detailed account, or even a review, of the ample material that may be brought to bear upon these matters. I desire, however, to state this clearly at the outset, because I am sure that in the presence of the vast number of observations that have been made, especially during the past few years, nothing short of a very extended treatise could be made to fairly represent the whole subject. Fortunately, my task is limited by the title of my paper, but I find myself at the same time in the difficult position of one who is called upon to define the proper limits of the subject, or, in other words, to mark out the debatable ground.

In doing this, I have thought it desirable to direct the attention of the Section chiefly to a certain number of important topics bearing upon the subject, as in this way we can get a better idea of its present status, and I have naturally included among the topics those with regard to which I have had the most personal experience.

It is a matter of regret that I shall be obliged to omit many facts of historical interest, as well as the names of well-known men, who, like Pasteur, Sanderson, Salisbury, and others, have enriched the field by original research. I shall also have to run the risk of appearing dogmatic, in assuming that certain questions have virtually been settled, or that others do not concern us. I shall thus take it for granted that the minute, vegetable organisms, called bacteria, exist pretty generally in nature, both in and out of the body; and, following the acceptance of this idea, that the question of spontaneous generation need not be introduced into the present matter in hand.

Almost any one, who for the first time follows the discussions on these subjects, encounters a little difficulty in the word *germ*, which is, perhaps, not a happy one to have come into use as expressing that from which a disease is derived. This, however, is its true meaning, and

neither indicates a vegetable nor an animal character, nor even that it is living, though this latter notion is held by Beale.<sup>1</sup> For even should a disease-poison turn out to be a chemical substance, the term "germ" is equally applicable to it, according to the proper definition of the word. In fact, under this threefold character, we are called upon to study these active principles, for about these three possibilities, of a vegetable, an animal, or a chemical, character, are grouped the three prominent theories that have been framed to explain the origin of infective diseases. These theories, or hypotheses, as they might be more properly called, are (1) the vegetable-germ, (2) the bioplasm, and (3) the physico-chemical, theory. The infective diseases are such, in a general sense, as are either propagated by direct contact, or through the medium of the air, various gases, fluids, or common objects. Inquiries have mostly been directed to such of these as are called septic, viz., erysipelas, pyæmia, septicæmia, and puerperal fever, and to others known as contagious, miasmatic, and the like, such as smallpox and typhoid fever.

I shall try to sketch these theories briefly:—

I. The "vegetable-germ theory" is the one that heretofore has attracted more attention and interest than any other. Though we have known it under this name for only a comparatively short time, it is not of recent origin, and has in reality been recognized from very early times in the history of medicine. It was at first, of course, merely a hypothesis of the flimsiest character, though it soon came to be regarded as a possible one, when the microscope showed that both animal and vegetable organisms, of exceedingly minute size, lived and grew in the interior of the body.

More color was given to this theory by the labors of Schwann, Cagniard de Latour, and Kützing,<sup>2</sup> who found that in fermenting matters there was a growth and multiplication of minute organisms, which they regarded as vegetable; when at a later period Pasteur<sup>3</sup> asserted that these particles were conditions essential to fermentation, then it came to be assumed that the phenomena of disease, which in many respects resembled them, might be due to an analogous cause. It was in this way that the doctrine of vegetable germs as the cause of disease came to be regarded as having good *à priori* evidence in its favor. This belief was further strengthened by Schönlein, who, in 1838, published his account of the fungus plant found in Favus, which is now almost universally believed to be caused by the deposit and development of the plant in the diseased part. As further investigations were made, the silk-worm disease, and the potato-rot, or murrain, were also admitted to be caused by growths of a similar nature.

More recently it has been held that a great many of the infective diseases have each a microphyte,<sup>4</sup> or minute, microscopic plant, as its peculiar active principle. These latter alleged discoveries have, however, been received with marked opposition, many excellent authorities refusing to accept these matters as definitely proved.

II. Other hypotheses had, therefore, to be brought forward, and prominent among them was that of Beale,<sup>5</sup> who, admitting that particles of

<sup>1</sup> Disease-Germs, p. 10.

<sup>2</sup> Schützenberger on Fermentations, pp. 36-7.

<sup>3</sup> Bastian; Lancet, April 10, 1875, p. 502.

<sup>4</sup> Such as the diphtheria-micrococcus of Letzerich, the cholera-fungus of Hallier, and the measles-fungus of Salisbury.

<sup>5</sup> Disease Germs, pp. 5 and 11.



minute size may produce disease, and in fact laying stress upon this point, believes that the particles in question are degraded portions of the animal body. Such particles he tells us have been seen by him, when using a sufficiently powerful lens, and he assures us that they divide and subdivide under suitable conditions, and "as living matters alone divide." Ross<sup>1</sup> has a modification of the same idea, and Hutchinson<sup>2</sup> states, with reference to certain diseases at least, such as gonorrhœa, purulent ophthalmia, erysipelas, and phagedæna, that they are due to the contagion of living cell-material, such as is called protoplasm, or bioplasm. These tenets, with more or less modification, are sustained by those who believe in the "bioplasm theory."

III. Bastian deserves to rank as the ablest exponent of the remaining theory, the "physico-chemical," or "physical." It is called a modification of Liebig's old theory, and, as now enunciated, holds that though minute organisms may act as ferments, they do so by virtue of chemical actions set up by them, while minute particles of the human body have almost an equal capacity for setting up diseased action under suitable circumstances. In either case, bacteria are apt to be engendered as correlative products.<sup>3</sup>

It will be noticed that two of these theories are based upon the belief that the origin of disease is due to minute particles, and that this belief does not militate against the third theory, and is admitted as possible by its advocates. This simplifies the matter before us very considerably, and enables us to state at once that these poisons are *particulate*, or certainly that they are apt to be bound up with particles.<sup>4</sup> I will merely add here that, in my experience, it may be possible that this has always been the case; some of the particles or molecules, may, of course, be almost immeasurably small.

We may get a good idea of the controversial points by considering first the arguments brought forward by those who support the vegetable-germ theory, and then the answers or explanations of its opponents.

(1) I have already stated that after the publication of Pasteur's brilliant experiments in relation to fermentation and putrefaction, they were regarded as affording good, *à priori* evidence of the truth of the doctrine now under consideration. But it must be remembered that, though sustained by the observations of many others, these views were strenuously opposed by Willis, Stahl, Liebig, and others, chiefly of the German school.<sup>5</sup> There is little doubt now that these latter were in a measure correct; in fact, Pasteur<sup>6</sup> has seen fit to modify some of his earlier statements, for he quite recently has said that both alcoholic fermentation and putrefaction may be initiated by the chemical processes taking place in the tissue-elements of certain fruits and vegetables, independently of the minute organisms supposed to be necessary to the process. Similar statements had previously been made by MM. Le Chartier and Bellamy, who found that, in modified forms of fermentation, independent organisms were generally absent at first, though they often made their appearance afterwards. Among the late contributors to this subject is Dougall,<sup>7</sup> who tells us that he has produced putrefaction without bacteria,

<sup>1</sup> British Medical Journal, May 27, 1876, p. 22.

<sup>2</sup> Ibid., April 24, 1875, p. 559.

<sup>3</sup> Lancet, April 10, 1875.

<sup>4</sup> There is excellent evidence of this in all the diseases which are alluded to in this paper.

<sup>5</sup> Schützenberger, p. 40.

<sup>6</sup> Lancet, April 10, 1875, p. 508; and Tribune Médicale, Avril 1, 1875, p. 321.

<sup>7</sup> British Medical Journal, April 24, 1875, p. 557.

and has seen bacteria without putrefaction—in which latter statement he can doubtless find many to accord with him.

Hiller<sup>1</sup> has also made statements to the same effect, for, having injected fresh eggs with a fluid containing bacteria, but not putrid, the eggs remained unaffected, which showed that bacteria might be present without decomposition ensuing. These views have been further supported by Donné and Beauchamp.<sup>2</sup> They are interesting, as showing that there has been, and still is, a diversity of opinion among scientific men as to the rôle which organisms play in fermentation and putrefaction. I may here add, also, that, in regard to the question of the ferment or cause of the ammoniacal decomposition of the urine, or fermentation, as it has been called, Pasteur<sup>3</sup> has stated definitely that it has not yet been demonstrated mathematically that the little torula to which he called attention several years ago, is the cause of the change, though he asserts that whenever putrid urine is examined the little plant is found.

(2) Another argument, commonly urged by those who believe in the vegetable-germ theory, is as follows: Almost all authorities admit that minute organisms may be the sole and sufficient cause of diseases such as scabies, favus, and the like, while many epidemic diseases among plants and animals are similarly produced, so that it is reasonable to suppose that vegetable organisms may be concerned in the production of infective diseases, the origin and propagation of which are thus explained with comparative ease. In reply, it is to be said that while no one may be willing to deny these facts, and while the silk-worm disease and potato-rot may be due to the vegetable particles that have been described; while various cereals may be affected with peculiar diseases, each exhibiting a peculiar plant; and while the pollen of many grasses may be the real cause of the hay-catarrh, or fever, as maintained by Blackley,<sup>4</sup> yet, that, on the other hand, it is certain that close observation in certain other directions shows the number of diseases due to vegetable growths to be really smaller than was formerly supposed. One has but to compare the long series of skin-diseases which but a short time ago were put down as caused by microphytes, with the modest list of five possible and three probable organisms, which are mentioned by a recent authority in these matters.<sup>5</sup> I refer to the Achorion of Favus, the Tricophyton of Tinea, and the Microsporon of Pityriasis versicolor.

The recent investigations of Lewis and Cunningham point in the same direction. They make it appear probable that in the Fungus-foot of India, the peculiar growth called Mycetoma is not necessary to the disease, as in some instances it has not been found, though the examinations were doubtless conducted with skill and care.<sup>6</sup> In the light of these and similar experiences, it would appear that while we are now and then discovering new plants or animals that act as disease-agents, we at the same time sometimes find that the number of such alleged causes of disease has been too large.

(3) It is further said that, in a number of the infective diseases, such as smallpox, typhoid fever, etc., there is a constant ratio between the intensity of the disease, in a given part, and the presence of bacteria; so that, where the disease is most active, bacteria are most numerous. This, indeed, is just what we should expect, in support of the vegetable-germ

<sup>1</sup> Centralblatt f. der med. Wiss., Dec. 1874.

<sup>2</sup> Schützenberger, p. 225.

<sup>4</sup> Experimental Researches on Hay Fever, 1873.

<sup>6</sup> Lancet, January 22, 1876.

<sup>3</sup> Loc. cit.

<sup>5</sup> Piffard, Diseases of the Skin.



theory, and it is a fact that few of its opponents are prepared to deny. But it has long ago been shown by Schwann and others,<sup>1</sup> and more recently by Tyndall,<sup>2</sup> that the air at times swarms with bacteria; and it is also true that bacteria occur in the body in health, the mucous membrane of the alimentary canal, from the mouth to the anus, having been found peopled by myriads of them in active, independent motion.<sup>3</sup> These facts have been so generally confirmed, that, as it may be remembered, I assumed them at the outset. Now bacteria are also found in the heart of the tissues, which is explained by the fact that they are taken up by the absorbents, and carried about, while they have, in a certain number of instances, been found in the blood of the lower animals, and sometimes in human blood.<sup>4</sup> Now, as long as this remains true, it is for those who maintain this theory to show that there is a manifest difference between the bacteria which they believe to be disease-agents, and those that we know are generally to be found in the tissues; for the mere fact that bacteria are found in extraordinary quantity at any one point, does not by any means indicate disease. In a large number of experiments, performed by Dr. Curtis and myself, it was found that, under certain circumstances not incompatible with ordinarily good health, vast collections of bacteria were to be found upon the tongue. Under these circumstances, it seems to me perfectly proper to believe that bacteria occur in the diseases just named as correlative products, and not as causes, of the disease. I may here venture to state that, as far as diphtheria is concerned, and upon this matter I have made some special study, I have never found any organisms connected with the disease that could in any way be distinguished from those found at other times in the body.<sup>5</sup> Of these experiments, I shall say more presently.

(4) Now, while it is further alleged that, in another class of diseases, such as erysipelas and pyæmia, septicæmia, puerperal fever, and hospital gangrene, there is always a numerical increase of bacteria at the points involved, we may be allowed to state, in this case also, that, the presence of bacteria in the body being allowed, their tendency to accumulate in diseased portions does not necessarily show that they have any relation with the cause of the disease; and when the question is further asked, how may we distinguish the bacteria of such diseases from each other, or from those of putrid infusions, I think that the same difficulty will be found as in the case of the other infective diseases, before mentioned.

(5) An important question is often asked, viz., Can any strictly chemical substance be a fever-producer, or do we know of any substance, whose chemical nature we can express by symbols, that can produce fever? This is a question usually put to those who advocate the physico-chemical theory of disease. It may be impossible to answer it affirmatively, and yet this by no means settles the matter. The minute chemistry of animal poisons is far from being as yet in a satisfactory condition, but we cannot therefore say that such substances may not at some time be found. Weir Mitchell,<sup>6</sup> of Philadelphia, in his most extensive researches on the poison of the rattlesnake, assures us that the poison is an albuminoid

<sup>1</sup> Beale and Sanderson.

<sup>2</sup> *Lancet*, May 8, 1875.

<sup>3</sup> Bastian, however, seems inclined to believe that these organisms do not come from the air.

<sup>4</sup> Wagstaffe and others.

<sup>5</sup> See Report on the Pathology of Diphtheria, in Report of the Board of Health of the City of New York, for 1877.

<sup>6</sup> Smithsonian Contribution, p. 46.



body (which he calls *crotaline*), which is not precipitated by boiling, but is by alcohol. Prince Bonaparte seems to have found, also, that the venom of the viper contains a similar, albuminoid substance, which he has called *echidnine*. Hiller<sup>1</sup> also believes that, in glycerine, he has found a material that has the power of extracting certain chemical poisons in putrid and septic matters. We see, therefore, that a certain definiteness has been reached in our estimation of a few active principles, and it is possible that when this field has been more actively worked by the chemist, we may find those other matters which the microscope has failed to analyze, and which yet may react in a definite way, so as to show individual characteristics. It is also reasonable to suppose that chemical combinations of more or less complexity may be formed in the body, under the influence of peculiar processes, or of the presence of virulent matter, and then, in either case, may communicate like qualities to other ordinary matter of the body; for the venom of serpents is certainly formed out of the normal tissue-elements. In the case of chemical compounds, they may increase to an indefinite amount when placed in suitable liquids, where the proper constituents are present.

(6) It is also maintained, by the vegetable-germ theorists, that the extraordinary capacity which disease-poisons have of retaining their vitality, is a strong argument in favor of their being bacteria, which resist various reagents, and exposure to extreme degrees of heat and cold, and which may remain dormant for long periods of time, without losing their capacity for reproduction. It is known, however, that the poison of the rattlesnake resists boiling, and is not rendered less virulent by alcohol; and Fayrer<sup>2</sup> has asserted that this latter quality belongs to the poison of the cobra; but both boiling and alcohol prevent the multiplication of bacteria, according to the testimony of so large a majority of observers that this point has seemed to me sufficiently settled. Whether or not minute particles of human tissue are capable of living long after separation from the body, is still a question before us, and not one that can just yet be summarily dismissed, as some would imply.<sup>3</sup> But if it should prove true that the little particles of living matter soon lose their capacity for reproduction, it does not follow that they have lost their power of acting in such a way as to communicate qualities to, or set up actions in, other particles. This is advocated by one who believes in the physico-chemical theory.

(7) Again, it is frequently urged by those who believe in the vegetable-germ theory, that the bacteria of certain diseases will induce like diseases in other persons or animals, when inoculated. This may be true in the case of individuals, though there is testimony against, as well as for, this assertion.<sup>4</sup>

I may here state that the results of my experiments and of those of Dr. Curtis, in regard to diphtheria, have failed to show that the inoculation of the bacteria of diphtheritic membranes upon *animals* produce any other lesions than those of bacteria artificially reared or obtained from our own mouths. Hiller<sup>5</sup> proposed to himself the following questions: whether (1) bacteria had the property of exciting inflammation, when inoculated? or (2) if in the blood did they produce fever? or (3) multiply? or (4) have the capacity of penetrating living organisms? He expe-

<sup>1</sup> Centralblatt f. Chir., 14, 15, 1876.

<sup>2</sup> Edinburgh Medical Journal, 1868 *et seq.*

<sup>4</sup> Compare the statements of Wolff, Küssner, and others.

<sup>5</sup> Allg. med. central Ztg., 1, 2, 1874.

<sup>3</sup> Sanderson.



rimented on animals, using the bacteria taken from different kinds of decomposing substances. The temperature rose, but not above 2° Fahr.; on the third day, the bacteria at the point of inoculation were shrivelled, and on the eighth day they had disappeared. Even when introduced into the living blood, they soon ceased to be recognized, though in blood exposed to the air they multiplied rapidly. In this connection, the experiment which Hiller made upon himself, the results of which he exhibited at last year's meeting of the German Surgical Society, deserves more than a passing notice.<sup>1</sup> He allowed himself to be punctured in eight places with bacteria, which he had isolated by a method of his own. When these punctures were exhibited at the Congress, six days afterwards, they had nearly healed, no traces of redness, inflammation, or pustule, remaining. He also showed another place where he had been subcutaneously inoculated three days before with a fluid containing bacteria. There had been local oedema, occurring six hours afterwards, but it had disappeared in forty-eight hours, and on the day in which he made his communication to the Society his general condition was excellent, his appetite was good, and he had no fever.

My own experiments on animals agree in a certain number of instances with those of Hiller. When the bacteria were filtered out of Cohn's nutrient fluid,<sup>2</sup> in which they are known to grow with exceeding rapidity, and were inoculated in the thighs of rabbits, the organisms ceased to be visible after the fourteenth day, though there was usually a marked deposit of a pasty material at the point of inoculation. The same thing was observed when inoculations were made with tongue-scrapings, or with diphtheritic membrane; the bacteria soon ceased to multiply, though the time at which the process stopped was variable; they became bloated and distorted, so that it was hard to make them out; after three weeks, they were rarely seen at all, though the focus of disease remained extensive, the animals quite often dying at a later date with symptoms of constitutional infection. Still, in all of these experiments it is not probable that the bacteria were ever completely isolated, for even when Cohn's fluid was used, where the only organic substance was the tartrate, fermentation took place, and some of the products of fermentation, perhaps in the form of minute particles, may have attached themselves to the bacteria which then may have been *carriers* of the poison—itsself a chemical product. And yet I have, in repeated instances, seen fluids inoculated upon rabbits, where the microscope showed bacteria in considerable numbers, though no trace of a lesion was observed.

We have now to consider a topic of great importance to us, in further defining our subject, and this is the classification of the organisms that are now called bacteria, to which class the vegetable-germ theorists, almost without exception, refer the agency of disease. Their name does not by any means imply that they are all rod-shaped, though the word *bacillum* means a little rod, but rather that they belong to a class of which the rod-shaped bodies are common types. Various classifications have been given of them, those of Billroth and Cohn having met with special favor, and each of these being tolerably complete. I will venture to say, however, that no elaborate classification appears to be necessary for these bodies, judging at least from our present knowledge of them, so that I

<sup>1</sup> Archiv f. klin. Chirurgie, 1875.

<sup>2</sup> Tartrate of ammonium, 1 gramme; phosphate of potassium, sulphate of magnesium, each, 5 decigrammes; phosphate of calcium, 5 centigrammes; distilled water, 100 cubic centimetres.

shall describe them by common terms, which can be as well understood by those who are not familiar with these matters as by those who have carefully studied them. Simple as the classification will be, it is perhaps convenient rather than accurate, for while it seems to me to cover the whole ground, it may be questioned whether it does not do more; *i. e.*, give a reality to some forms the existence of which is in doubt.

First we have (*a*) the very minute, round bodies, varying in size from those which are described as having a diameter so small that they can barely be seen by the ordinary high powers of the microscope, up to those which have a diameter of about  $\frac{1}{2500}$  of an inch: these are the Micrococci of Cohn, and the Microbacteria of Billroth; then we have (*b*) the little, oblong, or slightly oval, bodies that have a length of about one-third the diameter of a lymphoid corpuscle, and a breadth of about  $\frac{1}{2500}$  of an inch: they occur singly, or in chains of two or more elements; thirdly, there are (*c*) the little chains which often appear to be made up of minute spheroids; fourthly (*d*), the globular masses that appear to be made up of spherical bodies (*Zoogloea* of Cohn, Colonies of Hattier, *Gliacoccos* of Billroth); and fifthly (*e*), the filamentous bodies which are so often seen to glide about with an undulating or serpentine movement across the field of the microscope (*Spirilla* of Cohn).

I use the term bacteria for all these forms, and yet, as I have already said, objection may be made to this classification. It is held by some that the round particles known as micrococci, are nothing but either the rod-bacteria, seen end-wise, or merely particles of dead granular matter, or perhaps particles from the living protoplasm of cells. It is probably true that many mistakes of this kind have been made, and yet I should feel disinclined to believe that there are no round bacterial bodies, coming within the range already given, for it has seemed to me that the chains just described are composed of minute spheroids. As for the filamentous bodies known as spirilla, they are also thought by some to be composed of spheres. These bodies when single, or in segments, have two states, one of activity and one of rest; but mere absence of motion does not necessarily indicate that they have ceased to live, for under changed conditions they again resume their motions and multiply. All small spheroids have a motion within a limited area, but it is difficult, if not impossible, to distinguish in them that motion which is called "independent"—which is inherent in them as living particles, and is not caused by external circumstances. It has long been known that the mere fact of motion, in such particles, does not indicate life: for all particles are apt to show a kind of motion, which is greater in very fluid media, and less in dense media. These well-known facts, however, do not seem to be sufficiently prominent in the minds of some who have written on these subjects.

Real motion in such bodies may be certainly recognized, when they move against or across currents, and do not merely show irregular rotation or vibration in a limited area. The rod bacteria, chains, and long filaments, or spirilla, just described, have clearly this sort of motion, under certain conditions of life. The spirilla often dart across the field of the microscope, stop suddenly, and then dart back, or off in some new direction. Various micro-chemical methods have been devised for assisting the eye in detecting them. Among those that have claimed the most attention, are the methods of Letzerich, Eberth, and Hiller, all of which are more or less useful. Letzerich<sup>1</sup> employs a watery solution of

<sup>1</sup> Virchow's Archiv, lxii. 3, 1875.



iodine, which imparts to the rods and chains a deep-brown color; but Hiller has shown that this method is unreliable, from the fact that granular iodine is deposited, and that there are no means, *probably*, of distinguishing the iodine particles from the so-called spherical bacteria, or micrococci, etc., if such be present. The mere size of such atoms gives no criterion for determining their character, for, according to Cohn, the distinguished botanist, they vary in size within exceedingly wide limits. My own experience in using this method has inclined me to coincide entirely with Hiller.

Eberth's test consists in boiling the suspected bodies in alcohol, or in caustic alkalis, by which process the rods, chains, etc., are unaffected; but this method is objectionable from the fact that if we wish to get rid of all the oil, which resists these reagents a long while, the suspected tissue is itself apt to be destroyed.

The best method, in my experience, has been that of Hiller.<sup>1</sup> I have found the following modification of it to answer well: Make a ten per cent. watery solution of caustic potassa, in which the tissue to be examined is then immersed for an hour and a half, then washed in distilled water, and finally plunged into a mixture of tincture of iodine and distilled water, 1-25; after remaining in this menstruum for fifteen minutes, the substance assumes a brownish or deep-yellow color. The fatty matters are more or less dissolved, excepting, in some cases, the larger oil drops, but the bacteria retain the color more or less deeply. Such of the round, oily particles as remain after this treatment, can usually be distinguished from bacteria, by the fact that they refract the light strongly, while bacteria have a dull, lack-lustre appearance.

Sometimes we are called upon to decide as to the character of the dark substances that exist in cells, to determine whether they are bacteria or not. I at one time adopted a modification of this plan. In an instance where a rabbit had shown signs of constitutional disturbance after inoculation with putrid matter, I examined some of the blood on the second day after removal from the body, when bacteria were very plentiful, and when most of the white blood-corpuscles had disappeared, while those that remained were enlarged and granular. I added liquor sodæ in excess to a small amount of the blood, allowing it to act for one and a half hours. At that time the white corpuscles had swollen and were generally dissolved, liberating a large number of granules. Ten of these were kept in view, and moved about in all directions, turning and twisting; at one time they arranged themselves in a cluster, and then again separated, and formed a chain. During this time, the bacteria of rod-form had become more and more invisible; while these particular bodies, on the other hand, had become brighter and brighter. During all this time there was little or no change in a number of oil drops that were scattered about the field. Here, then, we have an instance of liquor sodæ having afforded us a means of differential diagnosis, in an optical manner, between bacterial bodies and certain particles that took the chain-form, and that came from the interior of white blood-corpuscles.

One of the most important reasons for putting little reliance on exact measurements as to the size and form of bacteria, is that these characteristics are probably apt to change under varying conditions. Bastian tells us that if we take an ordinary organic infusion, and expose it to a warm temperature, it will show rod-bacteria. If we add a drop of

<sup>1</sup> Virchow's Archiv, lxii., Jan. 1875.

acetic acid, we will get bacteria of larger size; adding a few drops more, the changes take place less rapidly, and the organisms, instead of multiplying as they did before, now grow continuously into filaments. This ground is said to be held by Trécul,<sup>1</sup> of Paris, and is favored by Beale;<sup>2</sup> my own experience is not sufficient to justify me in forming an opinion on this point. I may here add one point, viz., that I have seen no reason to believe that there is anything like a genetical relation between bacteria and the mould or sugar fungus.

I have already stated that my experience agrees with that of Chauveau and Sanderson, that the virulent principle is *particulate*, in certain instances at any rate. It is quite clear that very virulent fluids may be rendered quite harmless by passing them through a clay filter; this I have had repeated opportunities for observing, as far as relates to inoculation with putrid infusions, or with diphtheritic matter; and yet when we come to the question, *are these poisonous particles bacteria?* we know that by successive filtrations, as through paper, where the bacteria of distinctive forms are separated and removed, the fluid may still be poisonous. Granules are often observed in such fluids; *are they spherical bacteria, or the spores of these or others?*

We must remember, however, that rod- and chain-bacteria may be introduced in large numbers into the system without producing any lesion. When they *appear* to have been isolated, as in Cohn's fluid, this, as I have stated, is perhaps really not the case, but some organic compound may have attached itself to the vegetations, and thus have conveyed the septic influence.

Various efforts have at times been made to determine whether or not the poisonous matter is albuminoid. Chauveau, Onimus,<sup>3</sup> and Sanderson,<sup>4</sup> have worked in this direction. Sanderson and Onimus tried dialysis, and Chauveau diffusion. The former, in investigating the cause of the cattle plague, passed the virulent fluids through parchment-paper; the dialysate was wholly harmless, while the liquid that did not pass was poisonous. As the question with Sanderson was whether the contagia were crystalline or colloid, he decided in favor of the latter possibility. Onimus concluded that the matters were albuminoid from experiments conducted in much the same method. But there were in both sets of experiments, possibilities of error, arising from the fact that it was not certain whether albuminoid substances did not actually pass through the membranes, which it is now known that they will do, when certain quantities of the phosphates or carbonates happen to be present.<sup>5</sup> It would, therefore, be erroneous to conclude that the poison remaining behind the filter was necessarily albuminoid, when it was uncertain whether the harmless filtrate did not also contain albumen.

Chauveau appears to have shown, by his experiments, that it is extremely unlikely that the poison in vaccine virus is due to a soluble, albuminoid substance. His method will be briefly noticed. He took vaccine lymph, collected from the arm, and placed it in a test-tube standing in an upright position. The introduction of the lymph into the test-tube was effected with such care that the liquid did not touch the sides of the glass in the act of filling. Water, to the depth of a few

<sup>1</sup> Lancet, May 15, 1875, p. 684.

<sup>2</sup> Disease Germs, p. 37.

<sup>3</sup> London Medical Record, November 19, 1873.

<sup>4</sup> Twelfth Report of the Medical Officer of the Privy Council, 1869, p. 233.

<sup>5</sup> Graham, Proc. Royal Society, 1861, vol. ii, p. 243. I have not been able to refer to this paper.



lines, was then added with similar precautions, and the whole was allowed to stand for twenty-four hours. Although no membrane was used, yet it is said that when proper care was exercised, the liquids did not mix, except in the immediate neighborhood of the surface of junction. All the soluble constituents of the vaccine matter passed upwards into the water. At the end of twenty-four hours, the most superficial layer was removed by dipping into it the end of a fine capillary tube. This supernatant liquid was then examined microscopically, and tested for albumen. Now albumen, though held to have the least diffusibility of chemical compounds, was found in the water, the inference being that no other soluble chemical matter had been left behind. This upper stratum was used upon heifers and children, but without success, while the lower stratum produced the vaccine disease. Chauveau had previously employed a method called *sabaissement*, in which, by adding ten volumes of water, he had found that the leucocytes were separated. These did not produce the disease, but the stratum that produced infection contained minute, microscopic granules, and it was therefore concluded that the disease was produced by them. Sanderson corroborated these conclusions in the great majority of his attempts, though he experienced some difficulty in the required manipulations, which need a good deal of delicacy.

Colin<sup>1</sup> asserts that he has been unable to "diffuse," as Chauveau claims to have done, and intimates that the method is faulty, and that no such real diffusion takes place; Chauveau, however, insists that the granules, even when washed with immense quantities of water, retain their virulent quality, and compares them in this respect to the spermatie elements of seminal fluid. The supernatant liquid which is not poisonous, responds to the test for albumen by heat and nitric acid. In fact, Chauveau finds that the granules are as poisonous as the pus itself. According to Panum's<sup>2</sup> experiments, the virulent substance of putrid infusions is not destroyed by boiling, and is soluble in water, but not in alcohol; which qualities make him surmise that it may arise from the decomposition of albumen, or may perhaps be secreted from the bacteria, though he feels uncertain as to what the nature of the poison really is.

In prosecuting this line of inquiry, I have performed a number of experiments in co-operation with Dr. Edward Curtis, Professor of Materia Medica in the College of Physicians and Surgeons, New York, whose name I have previously mentioned in connection with other topics. The following questions were some of those that presented themselves for solution:—(1) Is the poisonous matter in putrid infusions destroyed by boiling and evaporation to dryness? (2) Is it soluble in alcohol, or not? (3) Is it soluble in water, after boiling in water and in absolute alcohol? (4) If there are granules in the fluid which prove poisonous, will they breed bacteria?

The liquid employed in these experiments was obtained from an infusion of a calf's liver, that had been allowed to become putrid; the liquids and solids used, were inserted into the muscular tissue of rabbits, and examined at varying times thereafter.<sup>3</sup> The following conclusions seemed in my opinion to be warranted:—

(1) Putrid matter, when introduced into the system, is capable of pro-

<sup>1</sup> La France Médicale, Fév. 26, 1876.

<sup>2</sup> Virchow's Archiv, lx. 3 and 4, 1874.

<sup>3</sup> Many of these experiments have already been reported. In fact, this entire paper embodies views which were published in 1875. Medical Record, Dec. 18 and 25, 1875.

ducing a well-marked train of symptoms, which are extraordinarily like those of ordinary *sepsis*.

(2) The poisonous quality does not reside in the absolutely clear liquid, when entirely freed from granules. This was shown by porous clay. The apparatus used in these experiments was devised by Dr. Curtis, and consisted of a porous-clay cylinder or cup, over the bottom of which was drawn a bit of rubber tubing, which was thick, and made to grasp the cylinder firmly; in the opposite end of this tubing was fitted a cork, through which a glass tube passed, so as to connect the chamber beneath the cylinder with the interior of a small glass jar that could be exhausted of air by means of a common exhausting syringe. When the liquid to be filtered was placed in the porous cylinder, and the air was removed from the glass jar, the liquid passed through the cylinder, and stood in beads or drops on its bottom, from which it was collected in small quantity without much difficulty.

(3) The poison is sometimes separated by coarse methods of filtration, such as by common filtering paper. When Cohn's fluid was passed through the equivalent of 25 thicknesses of ordinary filtering paper, it produced no lesion, and yet Cohn's fluid, unfiltered, and ordinary putrid infusions, produced about the same lesion.

(4) Continued boiling and evaporation to dryness does not destroy the poison.

(5) Continued boiling, and evaporation to dryness, and boiling with absolute alcohol, does not destroy the poison.

(6) The dry alcoholic extract, freed from alcohol by evaporation with heat, is poisonous.

(7) My experience with regard to the albuminoid character of the poison, has not made the matter clear to me, for while in these cases the dry alcoholic precipitate, after continued boiling, was poisonous and it contained the albuminoid substances, yet the liquid alcoholic extract in one case produced a lesion, and in another did not. In my first account of these experiments,<sup>1</sup> the results were stated as above, but in a subsequent series of experiments, the liquid alcoholic extract produced extensive lesions in two cases in which it was tried. In other words, when the albuminoid deposit produced by both boiling and alcohol was separated, and water afterwards added, the virulent matter appeared to reside both in the precipitate and supernatant fluid. These experiments do not, therefore, decide anything as to the albuminoid character of the poison.

(8) It further seemed to be shown of putrid matters which, after being filtered several times, were boiled to dryness, then boiled with absolute alcohol, and again dried and extracted with water, that the ordinary paper filtrate was poisonous.

(9) On examining this watery liquid, it was found to contain granules, and yet, when these granules were placed in *vacuum-tubes*, they in several instances failed to show any development of bacteria under such circumstances as favored the growth of bacteria. The suspected solution was put away in bent tubes, with suitable precautions, and while similarly arranged tubes that had been contaminated with the barest trace of bacteria, were found turbid from the production of these bodies seventy two hours afterwards, the suspected liquids were perfectly clear, with one exception, where there was a slight pellicle on the surface. It is true that, after a variable time, several tubes became contaminated, and yet

<sup>1</sup> Loc. cit.



others remained clear for months, and one for nearly a year, and as length of nozzle and fineness of neck are necessary conditions for success in the experiment, and as those thus provided held out best, it is fair to suppose that with the others some error was committed in carrying out the experiment, and that thus the bacteria of the air had in some way gained an entrance. That this is possible we have already seen.

It is proper now to stop here, and note that the granules have been very frequently noticed in the poisons of infectious disease; they seem destined to play an important part in the discussions now pending on the subject. There can be no question that in most of the diseases that are assumed to have a definite vegetable form as their immediate cause (for this is certainly the way in which the relation has been stated over and over again by the vegetable-germ theorists), authors have given the most conflicting accounts of the organisms, and we may fairly say that, with the exception of relapsing fever, not a single form has been accepted by any considerable number of germ-theorists as the agent, *par excellence*, of the disease. We have observed that, according to Chauveau, Sanderson, and Beale, certain granules appear to be associated with the origin of disease, and that this fact has been the point of departure of both the vegetable-germ theorists and the bioplasm theorists, while it is not incompatible with the physico-chemical theory. Let us examine these points a little more closely.

It is clear that if the vacuum-tube experiments be of value, they show that the particles observed are not the spores of bacteria. What evidence is there that the matter in question is organic and pertaining to the body? It is quite clear that, to the eye, using the ordinary powers of the microscope, these particles cannot be distinguished from one another with certainty. Beale,<sup>1</sup> however, assures us that by using extremely high powers, such as the  $\frac{1}{25}$  or the  $\frac{1}{50}$ , he has seen them at times dividing, and at others increasing in size, and that he has colored them with carmine. Some of these may, he says, be no more than  $\frac{1}{100,000}$  of an inch in diameter. In diseased conditions of the body, he believes that such particles may increase enormously. Belief in this doctrine is, of course, inconsistent with the old cell-doctrine, by which this body was regarded as the ultimate morphological element of the system; and yet we may safely say that this old theory is not by any means what Schleiden and Schwann once held.

It does not appear to be necessary that a cell should have an enveloping wall, inclosing a softer material in which is a nucleus. Max Schultze showed that many important cells possessed no cell-wall, and that some might not have a nucleus. Our notions, therefore, have been greatly modified in these respects, and a living cell is now held to be merely a mass of glutinous, viscid matter, which is endowed with peculiar qualities, called vital, such as amoeboid motion, molecular motion, and the like. As to the nature of this viscid substance, there is hardly much uniformity of opinion, as yet: some holding it to be formless and structureless, while others believe that it consists of networks, and others again, as Beale, that it is made up of minute spheres, closely packed together, and that these spheres may in turn be made up of other spheres. I hardly think, however, that microscopists are ready to agree upon any staining matter that is fitted to distinguish protoplasm or bioplasm in all cases, and these statements of Beale must, therefore, be accepted with caution. Even if

<sup>1</sup> Disease Germs, p. 246.

the particles be large, it is not certain that carmine will differentiate them. It has, to be sure, a preference for animal tissues, and yet it will also stain various other substances, if they remain long enough in the staining fluids. While, therefore, it is conceivable that the ultimate living elements of the body reside in particles which go to make up cells, we have no sure means of recognizing them, and of deciding positively that they are animal, and not vegetable, or whether or not they belong to that ill-defined class called granular matter. If, however, we believe that such minute portions of the body are the agents of disease, then we have to assume that they have a capacity for life which is remarkable: that, in fact, they can be subjected to extremes of heat and cold, or to the action of various acids and alkalies, and that they can be separated for months, and perhaps years, from the body, without losing their active qualities—all of which does not comport with the opinions commonly held about living animal matter.

The name "physico-chemical," as applied to the theory which is thus designated, is objectionable, as it dates back to the old-fashioned notions of Liebig, when the ideas held on these and kindred subjects were quite different from those of the present day. Liebig<sup>1</sup> held that the ferment was a portion of organic matter, which, itself unstable, was capable of communicating molecular movement (chemical change) to certain substances. Bastian, the exponent of the modified doctrine, holds, as already stated, that "living organisms, though they may act as ferments, act in this capacity merely by virtue of the chemical changes which the carrying away their growth necessitates, and that other chemical changes, taking place during the decay of organic matter, may make fragments of it (in the dead state) almost equally capable of initiating fermentative changes in suitable media."

This statement would appear to show that the friends of the theory are not altogether willing to deny to bacteria and allied forms, an influence in the cause of disease, but that they regard them as perhaps remote factors, the important one being the chemical change exerted by the growth of the microphytes, while, at the same time, dead organic matter may have a similar power. This theory is, therefore, properly a chemical one, and admits of two possibilities; either, on the one hand, that the cause of disease operates through chemical changes under the influence of minute organisms, or on the other hand, that it so operates under the influence of dead portions of the body. The former hypothesis is unlikely, because the virulence of diseases can sometimes be shown to be independent of bacteria; the latter one, however, is by no means impossible, though we know but little in its favor. If we assume that there is a logical connection between the processes of fermentation and disease, and decline to accept the hypothesis that minute organisms have that absolute *role* that has been given them, we may believe, with Hiller and others, that the ferment is a chemical substance. This is the view held by Bert with relation to vaccine virus, which he subjected to conditions under which life appeared to be impossible.

Under such an hypothesis, there is formed in the tissues, in certain diseases, a material which is able to resist various reagents (heat and cold, and the like), and which, when transferred to another organism, may occasion the formation of like compounds, just as the sulphate of sodium, instanced by Bastian, when placed in a liquid having the necessary ingredients for

<sup>1</sup> Lancet, April 10, 1875.



forming it, will increase in amount.<sup>1</sup> Now we actually know that the poisons of the cobra and of the rattlesnake, which are elaborated from healthy tissues, are capable of being subjected to conditions that are incompatible with life in its common acceptance. The poison of the cobra may be diluted with water, ammonia, or alcohol, without having its deadly qualities affected, while, according to Weir Mitchell,<sup>2</sup> the poison of the rattlesnake can be boiled or frozen, or subjected to the action of strong sulphuric or muriatic acid, ammonia, chlorine water, iodine, soda or potassa, and yet, as far as the matter has not burned, its virulence be unaffected. These qualities remind one strongly of the poison in putrid matters, where, according to my own and Panum's experiments, neither ordinary boiling in water, nor in absolute alcohol, nor evaporation to dryness, destroys its active qualities.

Let us glance, in conclusion, at the leading opinions at present entertained in regard to those of the infective diseases that have been most thoroughly studied with reference to the *materies morbi*. I shall refer merely to cholera, vaccinia, the carbuncular diseases of man and animals, typhoid and relapsing fevers, and diphtheria, in regard to which the most specific descriptions have been furnished of the organisms supposed to be concerned in their production.

The investigations which were occasioned by the *cholera* epidemic of 1849, appear to have been the first in which attention was called to certain particles, alleged to be the cause of the disease. These particles were called the cholera-fungus.<sup>3</sup> In 1867, Hallier<sup>4</sup> published a work in which he described the supposed ferment, the cholera micrococcus, a granular mass that by cultivation underwent a great variety of changes in form. Cohn<sup>5</sup> and many others followed with descriptions of the fungus. It is safe to say, however, that there has been no general agreement between the most prominent writers on this subject as to the specific form of the supposed contagium. In the Congressional report of the epidemic of 1873, in the United States, we find it stated<sup>6</sup> that no microscopic changes peculiar to cholera were found in the discharges, though high powers of the microscope were used; this being in agreement with the statement of Macnamara, who used a one-seventieth inch lens. Molecular matter was always seen by these observers, and it is stated in the report that from this molecular matter in the vibronic stage of decomposition, and not from the vibrones themselves, the dejecta of cholera patients are capable of setting up a morbid action in the intestinal canal of those who receive them.<sup>7</sup>

Among the most recent and complete experiments on this point are those of Lewis and Cunningham.<sup>8</sup> They injected 36 dogs, through the veins, with choleraic dejections. In 15 cases they obtained positive results: that is, death was evidently due to the matter injected. In 17 of the cases this matter had been kept for ten minutes at a temperature of 212° Fahr. In the remaining 19 cases it had not been exposed to heat. In the 17 cases the mortality was 47 per cent.; in the 19 others it was only 36 per cent. It was thus found that a continued temperature of 212° appeared to have no influence in abating the virulence of the matter, for, when it was boiled, the mortality was even a little greater than in the other cases. These observers also believed that bacteria could not

<sup>1</sup> Bastian, loc. cit.

<sup>2</sup> Budd and others.

<sup>3</sup> Biologie der Pflanzen.

<sup>4</sup> Ibid., p. 43.

<sup>5</sup> Smithsonian Contribution, p. 46.

<sup>6</sup> Das Cholera-Contagium.

<sup>7</sup> Report, etc., p. 36.

<sup>8</sup> Journal of Anatomy and Physiology.

be the cause of cholera, and in fact they found similar forms in the lesions produced by inoculation of various other substances, such as solutions of ordinary fæces, or urine.<sup>1</sup>

About ten years ago, it was noticed that *vaccine* virus contained minute spheroids, and they were described in 1867-1868.<sup>2</sup> Cohn called them *Microsphæra vaccinia*, and described them as small, colorless cells, sometimes in rosary-like chains of eight or more links, and sometimes clustered together. Sanderson thought that they were "filamentous, not jointed, but branching, and giving off from their extremities microspheres or conidia, much after the fashion of the penicillium."<sup>3</sup> Having been favored by Dr. F. P. Foster, Director of the Vaccine Department of the New York Dispensary, with an opportunity of inoculating calves, I performed the following experiment in relation to this matter. Having prepared a solution of salicylic acid, with sodium phosphate as a solvent, I combined it with equal parts of vaccine virus taken immediately from fresh vesicles, and having allowed the two to remain in contact a minute, they were inoculated in my presence, on a calf, in the usual way. Now this proportion of salicylic acid ( $\frac{1}{3}$  to  $\frac{1}{6}$ ) had been shown by previous experiment to be able to prevent the development of bacteria for from twelve to twenty-five days, and yet in this instance regular vesicles appeared at the proper time in nearly all the inoculated points. I cannot but think, therefore, that this experiment offers strong evidence against the theory that vegetable germs have to do with the cause of disease.

The name *Carbuncular Diseases*, which the French employ synonymously with the German word *Anthrax*, has proved to be a convenient form for a rather remarkable group of contagious diseases, which have a certain connection with one another, and which include malignant pustule, splenic fever, and the disease called "mycosis intestinalis." The post-mortem appearances in all these diseases are remarkably similar. Balls of rounded particles are said to be found in the affected parts, and rod-shaped bacteria in the circulating blood; the spleen is enlarged; there are hemorrhagic infarctions of the intestine, causing sloughing of the mucous membrane, exudation and infiltration of serum, and enlargement of the glands near the points involved. In such cases a pustule often appears, and hence the name Malignant Pustule; and yet it may not be necessary to the disease, which often proves fatal without it. Now, in these diseases, Pollender and Davaine<sup>3</sup> observed minute rods, which Davaine called bacteridia, and which he said were always motionless; and he has made such extensive studies of them that his opinions have become well known. He regarded them as necessary causes of the diseases in question, and as essentially different from what he called the bacteridia of decomposition, which were really what we know as the bacteria of putrid matters. His views have, however, not always met with acceptance, and notably have been opposed by Bouley,<sup>4</sup> Gaillard, and others, who assert that the blood may be infectious without the presence of rods. Bodinger, who is now regarded as one of the foremost German authorities, states that he also has produced the disease in question in a similar way, but that in such cases there have always been spherical bacteria present. We may justly ask, in view of what has already been cited, whether spherical bacteria were really present, and whether the particles he describes may not have been other solid particles?

<sup>1</sup> Tribune Médicale, 369, 1875.

<sup>2</sup> Virchow's Archiv, 41, 42, 1867-8.

<sup>3</sup> Davaine in 1850, and Pollender several years previously.

Cyclopædia of Practical Medicine, vol. iii. p. 377.



Among the most recent and best recorded accounts of the vegetable organisms connected with *typhoid fever*, are those of Klein,<sup>1</sup> of London. He declares that he has found peculiar bodies, in this disease, at or near Peyer's patches. These bodies were carried along the lymphatics or bloodvessels of the mucous membrane; in color they were often yellowish-brown, and in size varied from one-fourth to three times the size of a human, red blood-corpuscle. It will be noted that if we accept these views, we are carried away from the subject of bacteria towards that of the other vegetable organisms, called *torulæ*, which in my opinion have not been shown to have any genetical relation with bacteria. These views of Klein are comparatively new, and as yet I have failed to find any confirmation of them.

In regard to *relapsing fever*, the microphytes are pictured with more vividness than in any other disease. In 1872, Obermeier, of Berlin, gave an account of certain bodies, long and filamentous in form, which were found in the blood during the rise of the fever, disappearing with its fall, and reappearing during the relapse. These observations have been very largely confirmed, but, on the other hand, Laptschinski made frequent searches for these bodies, but never found them, though he did observe an enormous increase in the number of the white blood-corpuscles, which were unusually granular; when the fever decreased, the number of the white blood-corpuscles diminished. Recently, Heydenreich,<sup>2</sup> of Moscow, examined the blood in sixty-four cases, and he asserts that he found the spirillum in every instance, and that it was the same as the *Spirochaete plicabilis*, of Ehrenberg, which this observer discovered in water. In most cases these bacteria were found at the beginning of the febrile exacerbation, sometimes even preceding it. Before the fall of the temperature, the bacteria generally disappeared. On the other hand, we are told by Motschutkoffsky,<sup>3</sup> of Odessa, that the blood of relapsing-fever patients was readily and successfully inoculated upon healthy human subjects, though not on animals. The blood was only poisonous when it was taken during a febrile exacerbation, but it made no difference whether it contained spirilla or not.

In the matter of *diphtheria*, I may speak with more confidence, as my personal experience in this department of the subject is larger than in any other. The relation of bacteria to diphtheria has been made most prominent by the writings of Oertel, Hueter, and others; and, in conjunction with Dr. Edward Curtis, I have made some extended researches on the subject. Oertel, and others of the German school, plainly ascribe to the micrococcus found in diphtheria, the cause of the disease; at least I can understand them to imply nothing else. In the first instance, it must be said that the real presence of bacteria in diphtheritic membrane is usually a matter of ready proof. They exist in collections on the surface of the membrane, and often in it, as well as in the secretions of the pharynx, trachea, nasal passages, etc. They are to be found in masses, or separate, and usually may be distinguished as rod-shaped. It is true that they often appear as spheres, but this appearance is apt to be deceptive, for, when they are accumulated together, they are often arranged in extremely regular order, and they then give this peculiar appearance. To show that in such cases they are rods, is not a matter of much difficulty: Press the cover against the slide, and the

<sup>1</sup> Report of the Medical Officer of the Privy Council, 1875.

<sup>2</sup> St. Petersburger med. Wochenschrift, 1, 1876.

<sup>3</sup> Centralblatt, and St. Louis Medical and Surgical Journal, May, 1876.



more prominent rods will be pressed down, showing their peculiar shape. Another source of deception is the fact that these bacteria are apt to move about with a gyratory motion, with extremity directed towards the observer. Watching such a particle carefully, it may sometimes be seen to turn and expose its side, and then we may see that it is nothing but the ordinary rod-bacterium. When we have to do with other particles, then indeed it is well to give diagnostic points by which we may distinguish them from ordinary granular matter, such as fragments of tissue, minute oil particles, pigmentary matter, etc. I feel confident, however, from repeated examinations, that no particles have been described by Oertel as micrococci, that can be positively shown to be present in diphtheria alone. On the contrary, both Dr. Curtis and myself have repeatedly examined the accumulations in our own mouths, and have there seen the forms which are described as belonging to diphtheria.

And yet diphtheritic membrane is very poisonous, and fatal when inoculated in the muscles of rabbits, as I have had repeated opportunities of observing. I may here state that Oertel's descriptions are the most elaborate and, perhaps, the most clearly given of any writer's on the experimental pathology of diphtheria; as far, however, as my experience has gone, it has in most instances failed to verify them. In inoculating the corneæ of rabbits, in a number of instances, no lesion followed, beyond an ordinary keratitis, and none of the rabbits died; in fact they all recovered quickly. The fresh diphtheritic membrane, when inoculated, was very fatal, the tendency to death being extremely common about the end of the second day. Of 27 rabbits inoculated with the solid membrane, or an aqueous infusion of it, 20 died, and 12 at about the end of the second day, or between the second and third.

Now the membrane when thoroughly boiled, was equally fatal in two cases, and yet boiling is said by most excellent authorities to destroy bacteria. In fact, this is a matter of general belief. Furthermore, bacteria were shown to decrease rather than increase, when introduced into the system, so that certainly after two or three weeks they had either become distorted, so as to be hardly recognized, or they had altogether disappeared. When very strong solutions of salicylic acid, combined with phosphate of sodium as a solvent, were made up into a paste with diphtheritic membrane, and inoculated in the thighs of rabbits, they produced a fatal disease, though the lesions were not as extensive as when diphtheritic membrane alone was used; and yet, in my experience, salicylic acid in the proportion of  $\frac{1}{8}$  to  $\frac{1}{16}$  has, as before mentioned, prevented the development of bacteria for from twelve to twenty-five days.

I believe that I have now given a tolerably fair account of the most prominent views entertained on the matter of disease-germs, and think that I am warranted in submitting the following conclusions with regard to the present status of the question:—

I. That, as far as inquiry has been made as to the nature of the active principles in infective diseases, it is probable that in a certain number the matter is particulate, or molecular in form.

II. That in regard to the causes of septicæmia, pyæmia, puerperal fever, erysipelas, and hospital gangrene, and those of cholera, vaccine-disease, the carbuncular diseases of men and animals, typhoid and relapsing fevers, and diphtheria, there is not satisfactory proof that they are necessarily connected with minute vegetable organisms.

III. That the real nature of these causes is still uncertain.





